REMARKS

The foregoing amendment cancels claims 9 and 12, amends claims 1, 6, 7, 10, 11, 13, 17, 45, 47, 48 and 59 and adds new claim 60. Pending in the application are claims 1-60, of which claims 1, 11, 17, 19, 32, 35, 40, 45, 53 and 59 are independent. Claims 4, 5, 8, 19-44, 51 and 53-58 are withdrawn pursuant to a Restriction Requirement. The following comments address all stated grounds for rejection and place the presently pending claims, as identified above, in condition for allowance.

Independent claim 1 is amended to specify that the capping module substrate forms a chamber and that the trapping filter includes a semipermeable membrane forming a side wall of the chamber, subject matter originally found in claim 6 and canceled claim 9. The semipermeable membrane is impermeable to the matrix but permeable to fluids. Independent claim 11 is similarly amended, including the subject matter of canceled claim 12. Independent claim 45 is also amended to specify that each molecular fractionation device includes a matrix disposed in a chamber having a sidewall defined by a trapping filter including a semipermeable membrane.

Claims 6, 7 and 13 are amended to specify that the connector ports extend through the semipermeable membrane.

Consequential amendments are made to claim 10 in view of the changes to claim 1 and 9 but are not for purposes of patentability.

Independent claim 17 is amended to specify that molecular fractionation device includes four connector ports for placing the region holding the matrix into communication with a corresponding microchannel, each including a valve for selectively blocking fluid flow therethrough.

Independent claim 59 is amended to specify that the trapping filter includes a semipermeable membrane and that the device further includes at least one valve for selectively blocking fluid flow through one of the connector ports. *No new matter is added.*

Amendment and/or cancellation of the claims is not to be construed as an acquiescence to any of the objections/rejections set forth in the instant Office Action, and were done solely to expedite prosecution of the application. Applicants reserve the right to pursue the claims as originally filed, or similar claims, in this or one or more subsequent patent applications.

35 U.S.C. §102 Rejections

Applicants thank the Examiner for the close review of the claims and for indicating that claim 10 recites patentable subject matter. In the Office Action, the Examiner rejects claims 1-3, 6, 7, 9, 11-18 and 59 under 35 U.S.C. §102(b) as being anticipated by Wilding (U.S. Patent Number 5,498,392). The Examiner rejects claims 45-48 and 52 under 35 U.S.C. §102(e) as being anticipated by the Geli reference (U.S. Patent Publication Number 2003/0027354). The amendments to the claims traverse the rejections and place claims 1-3, 6, 7, 9, 11-18, 45-48, 52 and 59 in condition for allowance.

The present invention is directed to a molecular fractionation device that may be removably coupled to a microfluidic substrate to integrate a microfluidic function into microfluidic substrate without requiring significant modification of the substrate. As set forth in the specification, the terms "cap" and "capping module" refer to a structure having a microfluidic element, such as a matrix as set forth in the present claims, that is configured to stack on or communicate with a substrate to fully or partially complete a fluid path. The term "substrate" refers to a support structure having channels formed therein for conveying a fluid. The use of a self-contained capping module including a microfluidic element that can be added to a substrate by merely stacking the capping module onto a substrate provides significant advantages, such as ease of use, the ability to modify or exchange the capping module, a compact design, and so on.

The cited reference, alone or in combination, do not disclose or suggest the claimed molecular fractionation device or claimed use thereof. In particular, the cited references do not disclose a molecular fractionation device formed in a capping module that includes a semipermeable membrane forming a trapping filter defining a side wall of a chamber in the capping module for compartmentalizing a matrix thereon, as set forth in claims 1-16 and 19-59

The cited references also fail to disclose a molecular fractionation device including four *valved* connector ports for placing a region or chamber containing a matrix into communication with a corresponding microchannel, as set forth in independent claims 17 and 59. The use of a molecular fractionation device including four connector ports, which may have valves for selectively blocking the flow of fluid through each respective connector port, enables separation and capture or elution of a sample using a separate buffer, multi-dimensional fractionation of samples, separation of sample fractions into a plurality of different flow streams, and other processes that employ multiple flow paths through a chamber or region holding a matrix. The cited references do not disclose multiple flow paths through a chamber or region holding a matrix that is created by using four ports.

For example, the Wilding '392 reference, which the Examiner considers to anticipate claims 1-8, 11, 15-26, 32, 33, 35, 37 and 59, does not disclose a molecular fractionation device including a *semipermeable* membrane forming a side wall of a chamber in which a matrix is compartmentalized. Rather, all side walls in the chamber 22c wherein the beads 92 are disposed are solid walls formed of silicon, glass or plastic.

The Wilding '392 reference also fails to disclose a molecular fractionation device including four ports into a chamber or region holding a matrix, or ports interfacing with a chamber or region holding a matrix including valves for selectively blocking flow through the port. Rather, in Wilding '392, the chamber 22c wherein the beads 92 are disposed includes a single inlet to channel 20c and a single outlet to port 16D forming a single flow path through the chamber 22c. The ports 16A, 16B, 16C and 16D in the substrate 14 of Wilding '392 are not ports to the *region or chamber where the matrix is disposed*, and do not allow for fractionation of a sample by elution using multiple flow paths, as set forth in the present invention and shown in Figures 18A-28. Rather, the ports 16A, 16B, 16C, 16D interface with channels 24 in the device, one of which forms a single entry port to the chamber 22c.

Regarding claims 45-48 and 52, the Geli '354 reference discloses a device having microchannels fitted with a separation means in a selected segment. In the Geli '354 reference, the separation means is directly integrated with the chip, rather than being disposed in a separate structure that is coupled to the chip to integrate the matrix into the system. In addition, the Geli

reference does not disclose a semipermeable membrane forming a sidewall of a chamber of a molecular fractionation device for trapping a matrix therein. In fact, the Geli reference does not incorporate any type of membrane in any location on the device. Therefore, claims 45-48 and 52 also distinguish patentably over the Geli reference.

35 U.S.C. §103(a) Rejections

Claims 45-50 and 52 are rejected under 35 U.S.C. §103(a) as being unpatentable over the Wilding '392 reference in view of the Geli '354 reference. As recognized by the Examiner, the Wilding reference does not disclose a microfluidic system including a plurality of molecular fractionation devices coupled to a channel and arranged in series. According to the Examiner, because the Geli '354 reference discloses an outlet of a first microcolumn connected to an outlet of a second microcolumn, it would be obvious to modify the device of Wilding to include a plurality of molecular fractionation devices coupled to a channel and arranged in series.

Applicants respectfully disagree. There is no motivation to combine the teachings of the two references, as required under 35 U.S.C. §103(a). The Examiner has failed to provide an objective reason for combining the references and therefore fails to make a *prima facie* case of obviousness. Moreover, even in combination the references fail to disclose the claimed invention. Neither the Geli '354 reference nor the Wilding reference discloses a molecular fractionation device including a matrix disposed in a chamber having a sidewall defined by a trapping filter including a semipermeable membrane, as recited in independent claim 45. Therefore, claims 45-50 and 52 distinguish patentably over the combination of the Wilding reference and the Geli reference.

For at least these reasons, all pending claims of the present application are novel and include and inventive step over the cited prior art.

CONCLUSION

In view of the above amendment, applicants believe the pending application is in condition for allowance.

If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned attorney at (617) 227-7400.

Applicants believe no fee is due with this statement. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. TGZ-030 from which the undersigned is authorized to draw.

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Respectfully submitted,

By _____

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